UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/558,276	11/18/2005	Thomas Wisniewski	05986/100M536-US1	3691

26211 7590 01/13/2011
FISH & RICHARDSON P.C. (NY)
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
BOESEN, AGNIESZKA	

ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
01/13/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/558,276	WISNIEWSKI ET AL.	
	Examiner	Art Unit	
	AGNIESZKA BOESEN	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,9-13,15-20,22,23,28-31,33-37,40,45,46,51-53 and 56* is/are pending in the application.

4a) Of the above claim(s) *11-13,15-19,29-31,33-37 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,9,10,20,22,23,28,45,46,51-53 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/22/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed October 22, 2010 in response to the Office Action of July 23, 2010 is acknowledged and has been entered. Claims 11-13, 15-19, 29-31, 33-37, and 40 are withdrawn. Claims 1, 3-4, 9-10, 20, 22-23, 28, 45-46, 51-53 and 56 are under examination in this Office action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on October 22, 2010 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 102

Rejection of Claim 1 under 35 U.S.C. 102(a) as being anticipated by Sigurdsson et al. (American Journal of Immunology, 2002, Vol. 161, p. 13-17) **is withdrawn** in view of Applicant's arguments.

Rejection of Claim 1 under 35 U.S.C. 102(b) as being anticipated by Williamson et al. (PNAS, 1996, Vol. 93, p. 7279-7282) **is withdrawn** in view of Applicant's arguments.

Rejection of Claim 1 under 35 U.S.C. 102(b) as being anticipated by Prusiner et al. (US Patent 6,290,954 B1) **is withdrawn** in view of Applicant's arguments.

Claim Rejections - 35 USC § 103

Rejection of Claims 20, 28, 51 and 52 under 35 U.S.C. 103(a) as being unpatentable over Sigurdsson et al. (American Journal of Immunology, 2002, Vol. 161, p. 13-17) in alternative with Prusiner et al. (US Patent 6,290,954) and in alternative with Williamson et al. (PNAS, 1996, Vol. 93, p. 7279-7282) in view of Lu et al. (US Patent 5,733,760) and Chabalgoity et al.

(Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) and Grones (Biochemical and Biophysical Research Communications, 1995, Vol. 206, p. 942-947) **is withdrawn** in view of Applicant's arguments.

Rejection of Claims 3, 4, 22, 23 and 53 under 35 U.S.C. 103(a) as being unpatentable over Sigurdsson et al. (American Journal of Immunology, 2002, Vol. 161, p. 13-17) in alternative with Prusiner et al. (US Patent 6,290,954) and in alternative with Williamson et al. (PNAS, 1996, Vol. 93, p. 7279-7282) as applied to claims 1 and 20 in view of Lu et al. (US Patent 5,733,760) and Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) and further in view of Dunne et al. (US Patent Application Publication 2002/0194634 A1) and Benkirane et al. (Journal of Biological Chemistry, 1993, Vol. 268, p. 26279-26285, in IDS of 11/18/2005) **is withdrawn** in view of Applicant's arguments.

Rejection of Claims 9, 10 and 56 under 35 U.S.C. 103(a) as being unpatentable over Sigurdsson et al. (American Journal of Immunology, 2002, Vol. 161, p. 13-17) in alternative with Prusiner et al. (US Patent 6,290,954) and in alternative with Williamson et al. (PNAS, 1996, Vol. 93, p. 7279-7282) in view of Lu et al. (US Patent 5,733,760) and Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) in view of Clemens et al. (US Patent 6,440,423 B1) and Kleanthous et al. (US Patent 6,585,975 B1) **is withdrawn** in view of Applicant's arguments.

New Rejections

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Krasemann et al. (Journal of Immunological Methods, 1996, Vol. 199, p. 109-118) in view of Sigurdsson et al. (American Journal of Immunology, 2002, Vol. 161, p. 13-17).

Krasemann teaches a composition comprising recombinant non-infectious, non-pathogenic human prion protein resuspended in PBS and immunization of mice with the composition (see Subcloning, Plasmid preparation and Animals on page 111). It is noted that the present claims are product claims and the limitations regarding the intended use such as "suitable for mucosal administration" are not considered limiting. However, the composition disclosed by Krasemann is suitable for mucosal administration because the PBS is a pharmaceutically acceptable vehicle as evidenced by Krasemann. It is also noted that the present specification discloses mucosal immunization with the claimed composition resuspended in PBS ([87-88]). Thus the PBS resuspended prion protein disclosed in Kraseman is suitable for mucosal administration. Because the prior art composition and the claimed composition are non-infectious prion proteins resuspended in PBS, the prior art composition would be expected to elicit Th-2-type response associated with IgA humoral immune response, as required by the present claims.

Krasemann teaches human prion protein while the present claims are limited to mouse, bovine, deer, elk and sheep prion protein. Krasemann does not teach non-infectious mouse, bovine, deer, elk or sheep prion protein.

Sigurdsson teaches a composition comprising an isolated non-infections mouse prion protein and CFA adjuvant.

It would have been prima facie obvious to provide a composition suitable for mucosal administration comprising Sigurdsson mouse non-infectious prion protein and Krasemann's PBS.

The present claims would have been obvious because the substitution of one known element mouse non-infectious prion, taught by Sigurdsson for another human non-infectious prion, taught by Krasemann would have yielded predictable results to one of ordinary skill in the art at the time of the invention (i.e generation of the Th-2-type immune response associated with mucosal IgA humoral immune response). See KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007).

All the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 20, 28, 51 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krasemann et al. (Journal of Immunological Methods, 1996, Vol. 199, p. 109-118) in view of Sigurdsson et al. (American Journal of Immunology, 2002, Vol. 161, p. 13-17)as applied to claim 1 and further in view of Lu et al. (US Patent 5,733,760) and Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) and Grones (Biochemical and Biophysical Research Communications, 1995, Vol. 206, p. 942-947).

Kraseman and Sigurdsson teach a composition comprising isolated non-infectious, non-pathogenic mouse prion protein and PBS. Neither Krasemann nor Sigurdsson, teach Shigella or Salmonella transformed with a vector expressing non-infectious, non-pathogenic mouse prion protein.

Lu et al. teach vaccine compositions comprising attenuated Salmonella vectors expressing heterologous DNA encoding viral antigens from HIV and HCV viruses (see the entire document, particularly claims 1-9, column 5, lines 65-67, column 10, lines 19-60). While Lu et al. teach Salmonella typhi, Salmonella typhimurium, and Salmonella enteritidis, (see column 6, lines 65-67, Lu et al. does not teach the specific Salmonella strains as recited in the present claim 28.

Chabalgoity et al. teach Salmonella typhimurium LVR01 strain expressing heterologous antigens encoding binding fatty acid protein from Echinococcus granulosus (see the entire document, particularly Materials and Methods).

Grones teaches Shigella transformed with heterologous plasmids (see Results and Discussion).

It would have been prima facie obvious to express Krasemann and Sigurdsson's mouse prion protein in Lu's and Chabalgoity Salmonella bacterial vectors used for expression of heterologous antigens and to provide a composition comprising attenuated Salmonella typhi bacterium transfected spp strain transformed with a vector capable of expressing a mammalian prion protein.

One would have been motivated to express Krasemann and Sigurdsson's, mouse prion protein in Lu's attenuated Salmonella or in Grones' Shigella because Lu et al. teach that their Salmonella vectors are particularly effective for induction of mucosal protective immune responses against mucosally transmitted infectious agents. Lu et al. also teach that attenuated Salmonella vectors are effective vectors for delivery of desired antigens because the bacteria grow rapidly and do not require growth in cell culture, thus allowing large scale production of vectors (see column 1, lines 19-55).

One would have been motivated to use Chabalgoity's Salmonella typhimurium LVR01 because Chabalgoity et al. teach that heterologous antigens expressed in LVR01 effectively elicits humoral and cellular immune responses in animals (see the entire document, particularly Results and Discussion on page 468).

One would have had a reasonable expectation of success to provide a composition comprising an attenuated Salmonella typhi bacterium and particularly Salmonella typhimurium LVR01 transformed with a vector capable of expressing a mammalian prion protein because the technology used for generation of bacterial recombinant vectors has been available to the skilled artisan at the time of the present invention. Moreover, the bacterial recombinant vectors

expressing heterologous antigens have been successfully made in the art at the time of the invention as evidenced by Lu et al. and Chabalgoity et al.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 3, 4, 22, 23, 45-46 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krasemann et al. (Journal of Immunological Methods, 1996, Vol. 199, p. 109-118) in view of Sigurdsson et al. (American Journal of Immunology, 2002, Vol. 161, p. 13-17) as applied to claims 1 and 20 in view of Lu et al. (US Patent 5,733,760) and Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) and further in view of Dunne et al. (US Patent Application Publication 2002/0194634 A1) and Benkirane et al. (Journal of Biological Chemistry, 1993, Vol. 268, p. 26279-26285, in IDS of 11/18/2005).

Krasemann and Sigurdsson teach a composition comprising isolated non-infectious, non-pathogenic mouse prion protein. Neither Krasemann nor Sigurdsson teach SEQ ID NO: 4 or D-amino acids.

Dunne teaches present SEQ ID NO: 4 (see SEQ ID NO: 10).

Benkirane et al. teach that changing the amino acids within an antigenic peptide from an L-residue to the corresponding D-residue drastically increases the antigenicity of the peptide and contributes to the generation of high levels of IgG3 antibodies in immunized animals (see the entire document, particularly page 26279 and Discussion).

Thus based on the teaching of Benkirane et al., it would have been prima facie obvious to the person skilled in the art to provide a pharmaceutical composition designed for induction of

immune responses, wherein the amino acids within the antigenic protein are D-amino acids. It would have been prima facie obvious to the person skilled in the art to provide a pharmaceutical composition comprising Dunnes' s SEQ ID NO: 4 representing deer prion protein.

One would have been motivated to provide Krasemann and Sigurdsson's, pharmaceutical composition comprising mammalian prion protein wherein the amino acids of the prion protein are D-amino acids, because Benkrine et al. teach that changing the amino acids within an antigenic peptide from L- to D- amino acids results in increased antigenicity and thus better immunogenicity of the peptide.

One would have had a reasonable expectation of success to provide a composition comprising a mammalian prion protein wherein all amino acids are D-amino acids, because the means required for the synthesis of proteins containing D-amino acid residues have been available to the skilled artisan at the time of the present invention as evidenced by Benkriane et al.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 9, 10 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krasemann et al. (Journal of Immunological Methods, 1996, Vol. 199, p. 109-118) in view of Sigurdsson et al. (American Journal of Immunology, 2002, Vol. 161, p. 13-17) as applied to claim 1 and further in view of Lu et al. (US Patent 5,733,760) and Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) in view of Clemens et al. (US Patent 6,440,423 B1) and Kleanthous et al. (US Patent 6,585,975 B1).

Krasemann and Sigurdsson teach a composition comprising isolated non-infectious, non-pathogenic mouse prion protein. Neither Krasemann nor Sigurdsson teach the composition wherein the prion protein is covalently attached to the cholera toxin subunit B or aluminum hydroxide as a delivery vehicle.

Clemens et al. teach cholera toxin subunit B as an effective adjuvant comprised in vaccine compositions comprising viral or bacterial antigens (see the entire document, particularly claims 1-7 and column 4, lines 28-51). It is noted that Clemens et al. also teach another adjuvant species recited in claim 9, the heat-liable enterotoxin (LT) (see column 9, lines 60-67 and column 10, lines 1-67). Clemens et al. do not expressly teach covalent attachment of cholera toxin subunit B to the antigenic protein.

Kleanthous et al. teach covalent attachment of cholera toxin subunit B adjuvant to the antigenic protein (column 5, lines 1-20). Kleanthous et al. teach adjuvant aluminum hydroxide (see column 6, lines 3-8).

It would have been prima facie obvious to covalently attach cholera toxin subunit B to the prion protein. One would have been motivated to covalently attach Clemens' cholera toxin subunit B to Sigurdsson's mouse prion protein, because Clemens' teach that cholera toxin subunit B adjuvant allows for improved mode of oral immunization and development of serum and mucosal antibodies against pathogenic microorganisms and that the cholera toxin subunit B is useful in combination with any specific antigen where a specific neutralizing antibody response would be beneficial in ablating the disease state associated with the antigen (see column 9, lines 5-26).

One would have had a reasonable expectation of success to provide a pharmaceutical composition comprising prion protein covalently attached to the cholera toxin subunit B, because a covalent attachment of cholera toxin subunit B to antigens of interest has been successfully practiced in the art as evidenced by Kleanthous et al.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowed.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen/
Examiner, Art Unit 1648